ViewPoint™ CK System

PMA P010018

Presentation to
Ophthalmic Devices Advisory Panel

November 30, 2001

Refractec

Conductive Keratoplasty for Hyperopia

- Introduction
  - Judy Gordon, DVM - Regulatory Consultant
- Technology Overview
  - Jon Hayashida, OD - VP, Clinical Affairs
- Clinical Results:
  - Marguerite McDonald, MD - Medical Monitor and Clinical Investigator
  - Peter Hersh, MD - Clinical Investigator

Surgical Correction of Hyperopia

- Challenge of steepening the central cornea
- Current treatment modalities include excimer laser ablation of corneal periphery and shrinkage of collagen in a circular pattern in the corneal periphery

Collagen Shrinkage via Thermal Keratoplasty

- Alters corneal curvature by heating the stromal tissue causing collagen to shrink
- There is an optimal collagen shrinkage thermal profile
- Too low - minimal effect
- Too high - causes remodeling and regression of effect
- Two methods: application of laser energy and application of radio-frequency energy

ViewPoint™ CK System

Conductive Keratoplasty (CK)

- A controlled release of radio-frequency energy is delivered intra-stromally via a probe tip (450 X 90 microns)
- Impedance of the corneal tissue results in a thermal effect
- Thermal profile is homogeneous to approximately 80% the depth of the cornea

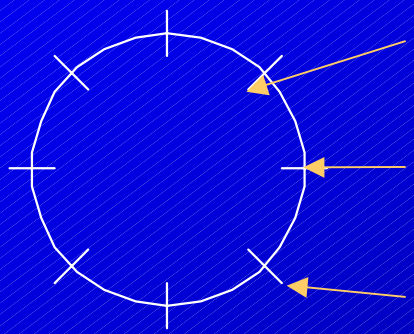
CK Footprint

Average width ~ 405 microns

Average depth ~ 509 microns

(measured by ultrasonic biomicroscopy)

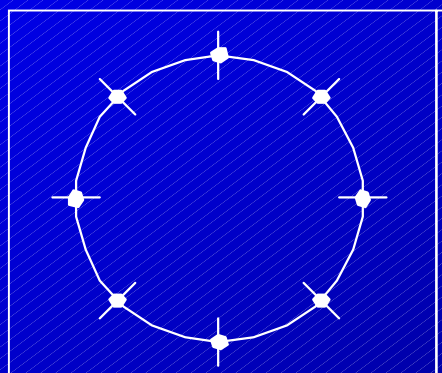
Nomogram



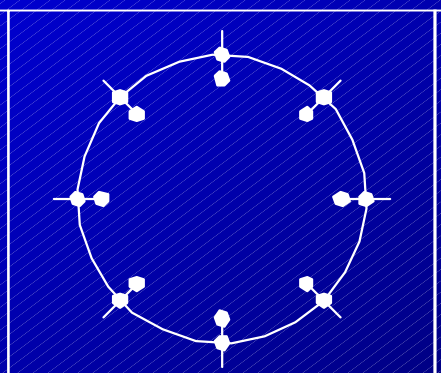
6 mm (inner hash mark)

7 mm (intersection of circle)

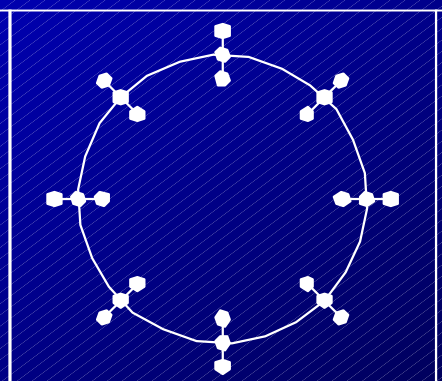
8 mm (outer hash mark)



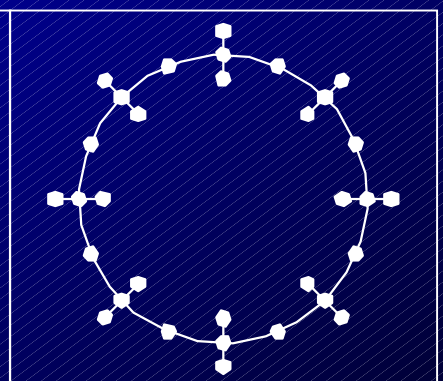
+0.75 to +0.87 D



+1.00 to +1.62 D

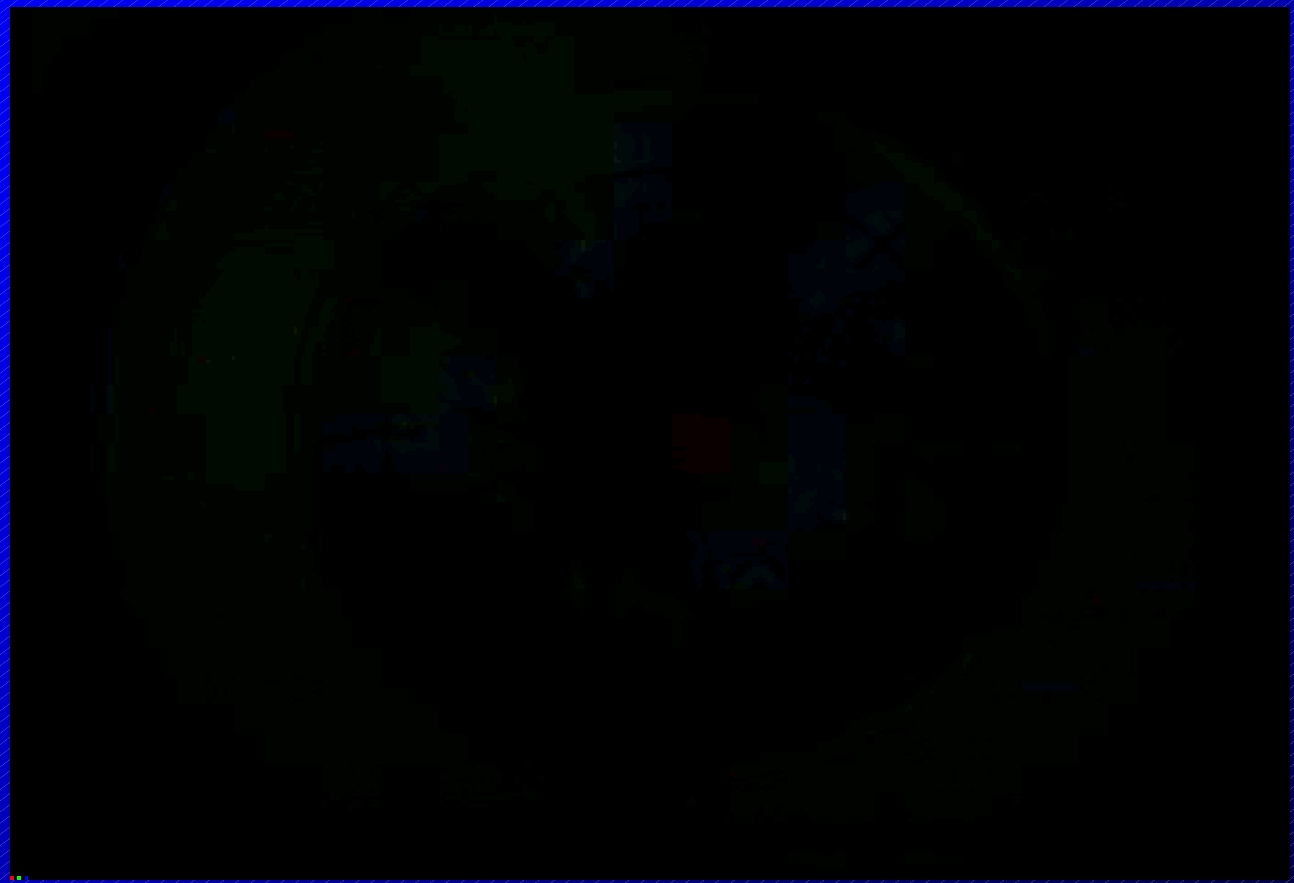


+1.75 to +2.25 D



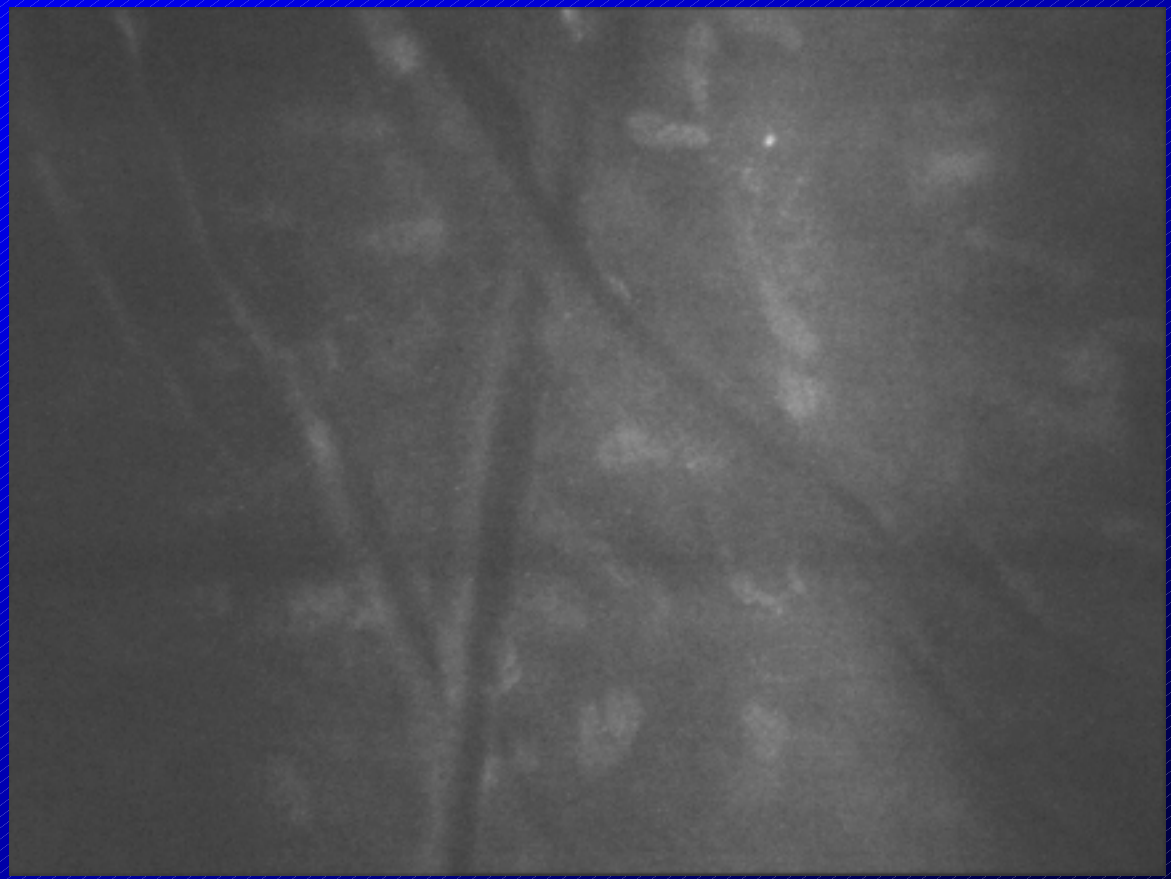
+2.37 to +3.00 D

Conductive Keratoplasty



Confocal View of CK

12 month confocal view of CK treated eye with folds between treatment spots



Sabry, McDonald & Klyce - 2001

Clinical Results

Marguerite McDonald, MD
Medical Monitor
and Clinical Investigator

Peter Hersh, MD
Clinical Investigator

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Protocol RCS-001-HYP

A Prospective Multicenter Clinical Trial to Evaluate the Safety and Effectiveness of the ViewPoint™ CK System for the Correction of Hyperopia Utilizing the Conductive™ Keratoplasty (CK) Procedure

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Clinical Investigators

- Penny Asbell, MD
  New York, NY
- Stephen Brint, MD
  Metairie, LA
- William Culbertson, MD
  Miami, FL
- Daniel Durrie, MD
  Overland Park, KS
- Bruce Grene, MD
  Wichita, KS
- Peter Hersh, MD
  Teaneck, NJ
- Vera Kowal, MD
  Rapid City, SD
- Richard Lindstrom, MD
  Minneapolis, MN
- Robert Maloney, MD
  Los Angeles, CA
- Edward Manche, MD
  Palo Alto, CA
- Marguerite McDonald, MD
  New Orleans, LA
- Alan Sugar, MD
  Ann Arbor, MI

Study Design

- Prospective, multicenter trial consistent with FDA Guidance for Refractive Surgery Lasers (September 1997) and draft ANSI Guidance for Laser Systems for Corneal Reshaping
- Full correction of spherical hyperopia, i.e., target of plano
- Eligibility
  - +0.75 to +3.25 D spherical hyperopia
  - - 0.75 D or less refractive cylinder
  - +0.75 to +3.00 D cycloplegic spherical equivalent
- All treatments based on preoperative cycloplegic refraction spherical equivalent (CRSE)

Effectiveness Parameters
Protocol RCS-001-HYP

- Improvement in UCVA
- Predictability
- Stability
- Patient satisfaction

Safety Parameters
Protocol RCS-001-HYP

- Preservation of BSCVA
- Induced cylinder
- Endothelial cell loss
- Patient symptoms
- Complications and adverse events

Demographics
All Eyes Enrolled
(401 eyes of 233 subjects)

Gender	Male	97	42%
	Female	136	58%
Race	Caucasian	188	81%
	Black	21	9%
	Asian	4	2%
	Other	20	9%
Age (years)	Mean	55.3	
	Range	40.2, 73.9	

Baseline Refractive Characteristics
All Eyes Enrolled
(n = 401)

	CRSE	MRSE
Mean (S.D.)	1.86 (0.628)	1.80 (0.637)
Range	0.75, 4.00*	-0.38,** 3.75

* Original protocol allowed for treatment of 1.00 to 4.00 D of cycloplegic spherical hyperopia

** Two ineligible eyes enrolled with > 0.5 D difference between MRSE and CRSE (MRSE –0.38, -0.12)

Preop Refractive Parameters by Diopter
All Eyes Enrolled
(n = 401)

Preop Spherical Equivalent	CRSE		MRSE	
	n	%	n	%
0.00 to 0.99 D	19	5%	25	6%
1.00 to 1.99 D	215	54%	215	54%
2.00 to 2.99 D	143	36%	147	37%
3.00 to 4.00 D*	24	6%	12	3%

* Original protocol allowed for treatment of 1.00 to 4.00 D of cycloplegic spherical hyperopia

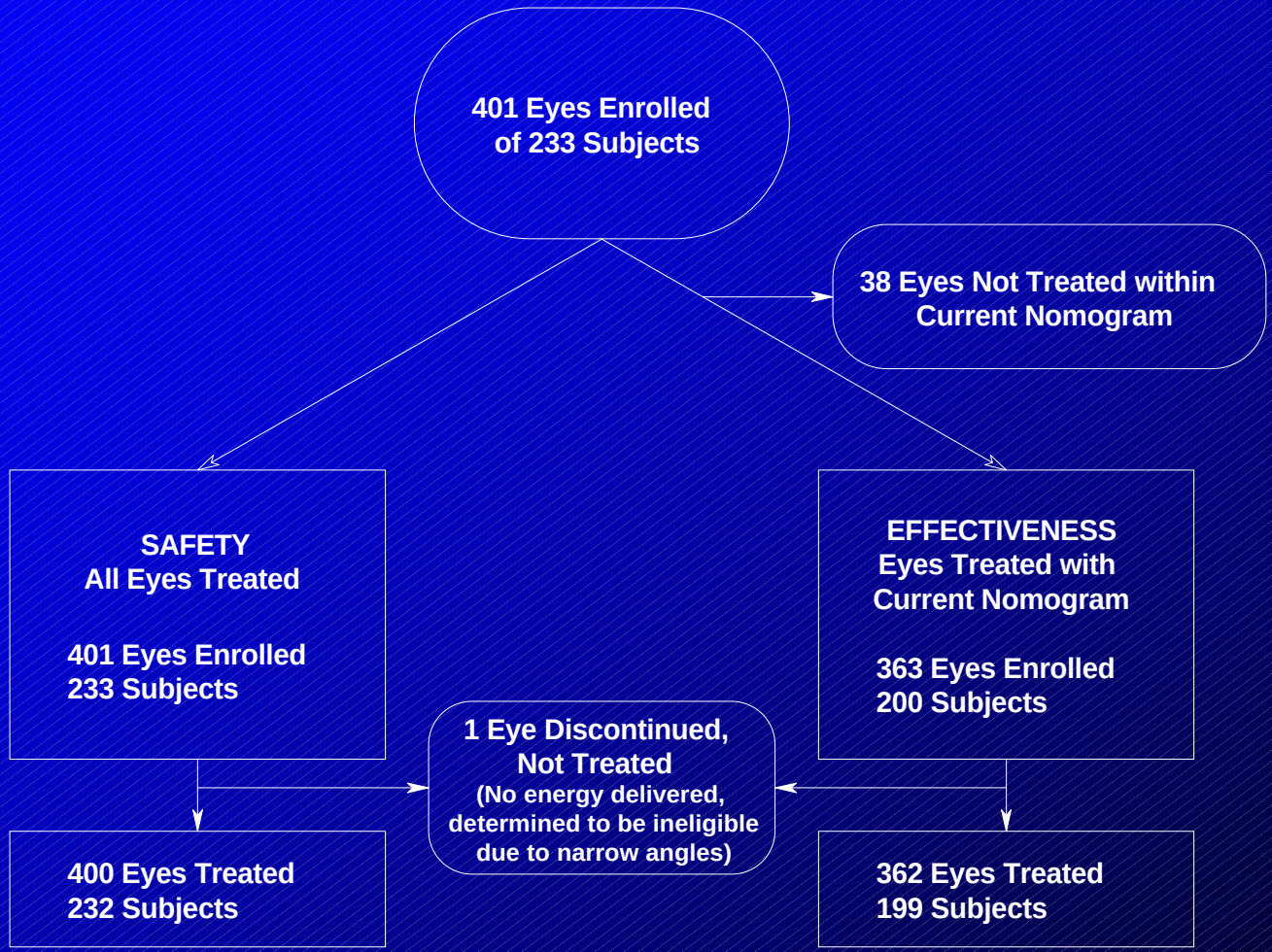
Nomogram Adjustment

- Analysis of first 54 eyes indicated overcorrection at the low end of the range and undercorrection at the upper end of the range
  - Reduction of maximum CK treatment range from 4.00 D to 3.25 D cycloplegic spherical hyperopia and CRSE ≤ 3.00 D
  - Addition of 8 spot treatment pattern
  - Revised treatment range and patterns identified as “current nomogram”

Accountability
All Eyes Enrolled

	1 Month	3 Months	6 Months	9 Months	12 Months
Enrolled	401	401	401	401	401
Not yet eligible for interval	0 0%	0 0%	2 <1%	12 3%	192 48%
Available for Analysis (in visit window)	390 97%	394 98%	387 97%	376 94%	203 51%
Discontinued/ Lost to Follow-up	1 <1%	1 <1%	1 <1%	3 1%	5 1%
Missed Visit	10 2%	6 1%	11 3%	10 2%	1 <1%
% Accountability	97% (390/401)	98% (394/401)	97% (387/399)	97% (376/389)	97% (203/209)

Study Cohorts



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Presentation of Results

- Effectiveness reported for eyes treated with current nomogram
- Safety and stability reported for all eyes treated

Effectiveness

Summary of Effectiveness
Eyes Treated with Current Nomogram

	6 Months (n = 350)	9 Months (n = 340)	12 Months (n = 171)	FDA Target
UCVA 20/20 or better	46%	50%	51%	-
UCVA 20/25 or better	65%	74%	73%	-
UCVA 20/40 or better	90%	93%	91%	85%
MRSE ≤ 0.50 D	61%	64%	58%	50%
MRSE ≤ 1.00 D	88%	87%	91%	75%
Stability				
Change in MRSE	Between 6 and 9 Months		Between 9 and 12 Months	
≤ 0.50 D	88%		85%	
≤ 0.75 D	95%		97%	
Mean Change per Month	0.03		0.04	

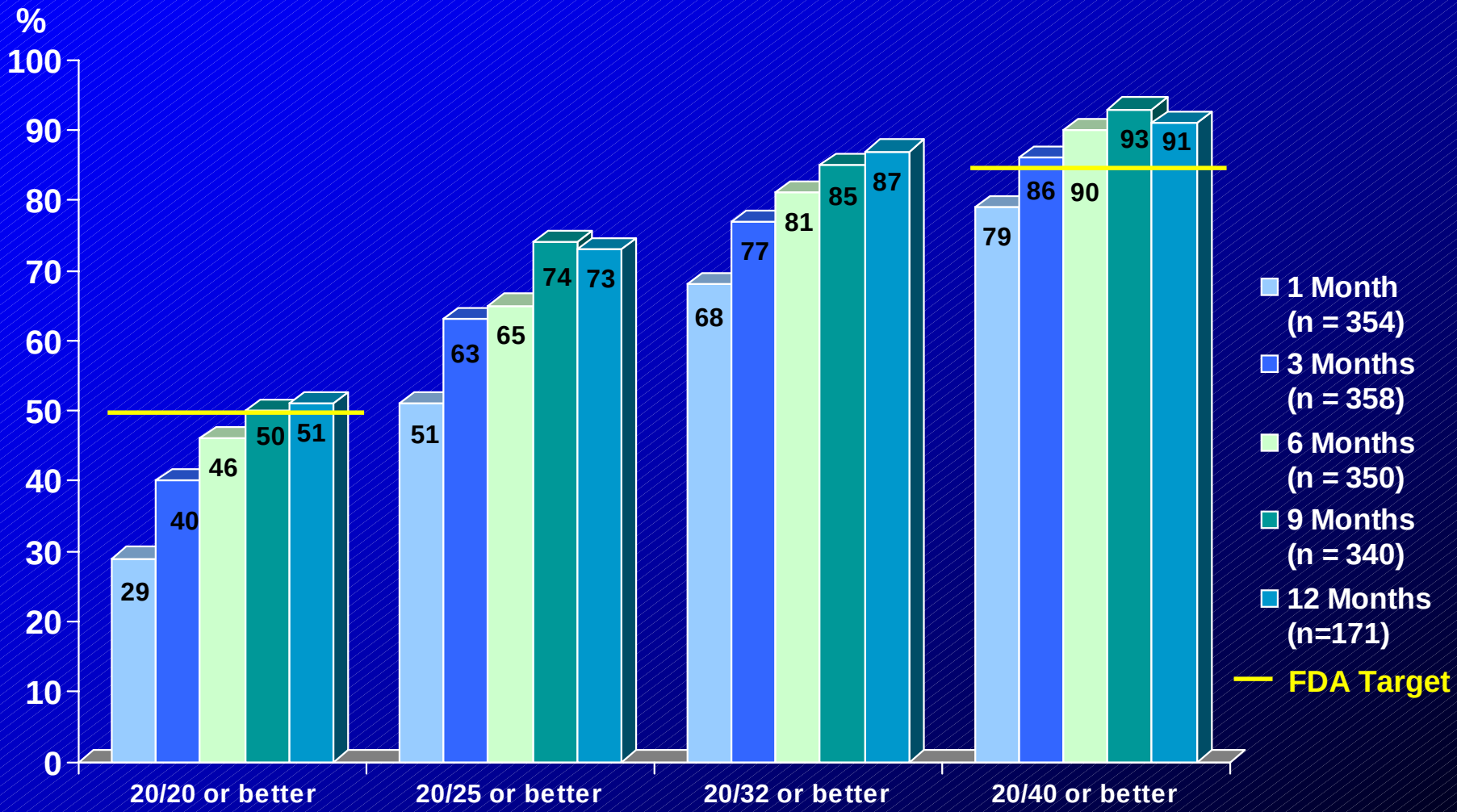
Effectiveness Parameters
Protocol RCS-001-HYP

- **Improvement in UCVA**
  - **UCVA 20/40 or better in ≥ 85% of eyes with preoperative BSCVA 20/20 or better**
- Predictability
- Stability
- Patient Satisfaction

Uncorrected Visual Acuity
Eyes Treated with Current Nomogram

	1 Month (n = 354)	3 Months (n = 358)	6 Months (n = 350)	9 Months (n = 340)	12 Months (n = 171)	FDA Target
UCVA 20/20 or better	29%	40%	46%	50%	51%	-
UCVA 20/25 or better	51%	63%	65%	74%	73%	-
UCVA 20/32 or better	68%	77%	81%	85%	87%	-
UCVA 20/40 or better	79%	86%	90%	93%	91%	85%

Uncorrected Visual Acuity
Eyes Treated with Current Nomogram



No retreatments performed during the study

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Postoperative UCVA vs. Preoperative BSCVA
(Paired Analysis at Last Reported Visit)

- Postoperative UCVA equal to or better than preoperative BSCVA for 32% of eyes
- Postoperative UCVA within 1 line of preoperative BSCVA for 63% of eyes

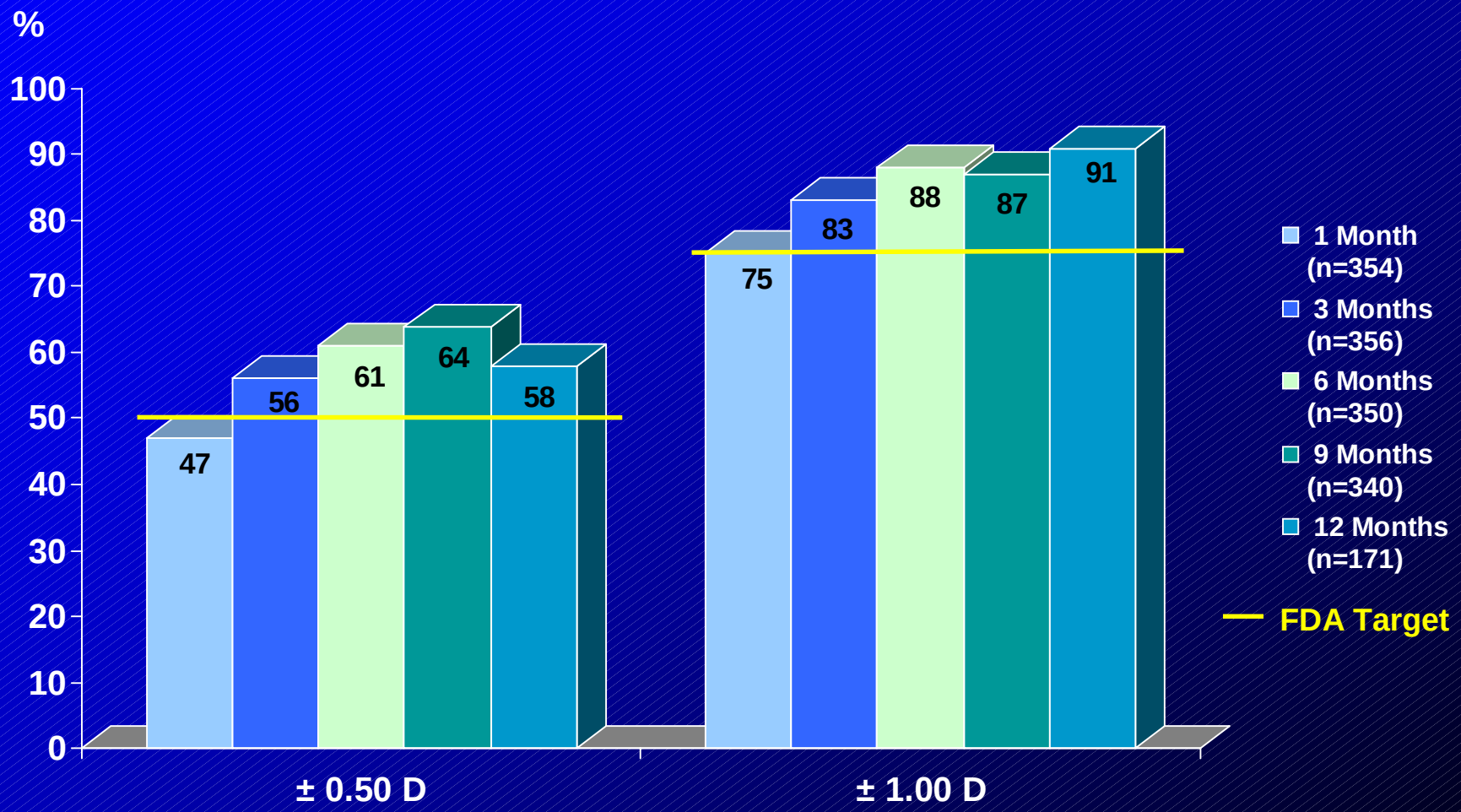
Effectiveness Parameters
Protocol RCS-001-HYP

- Improvement in UCVA
- **Predictability**
  - **MRSE within ± 0.50 D for 50% of eyes**
  - **MRSE within ± 1.00 D for 75% of eyes**
- Stability
- Patient Satisfaction

Accuracy of MRSE
Eyes Treated with Current Nomogram

MRSE	1 Month (n = 354)	3 Months (n = 356)	6 Months (n = 350)	9 Months (n = 340)	12 Months (n = 171)	FDA Target
± 0.50 D	47%	56%	61%	64%	58%	50%
± 1.00 D	75%	83%	88%	87%	91%	75%
± 2.00 D	94%	97%	99%	99%	99%	-

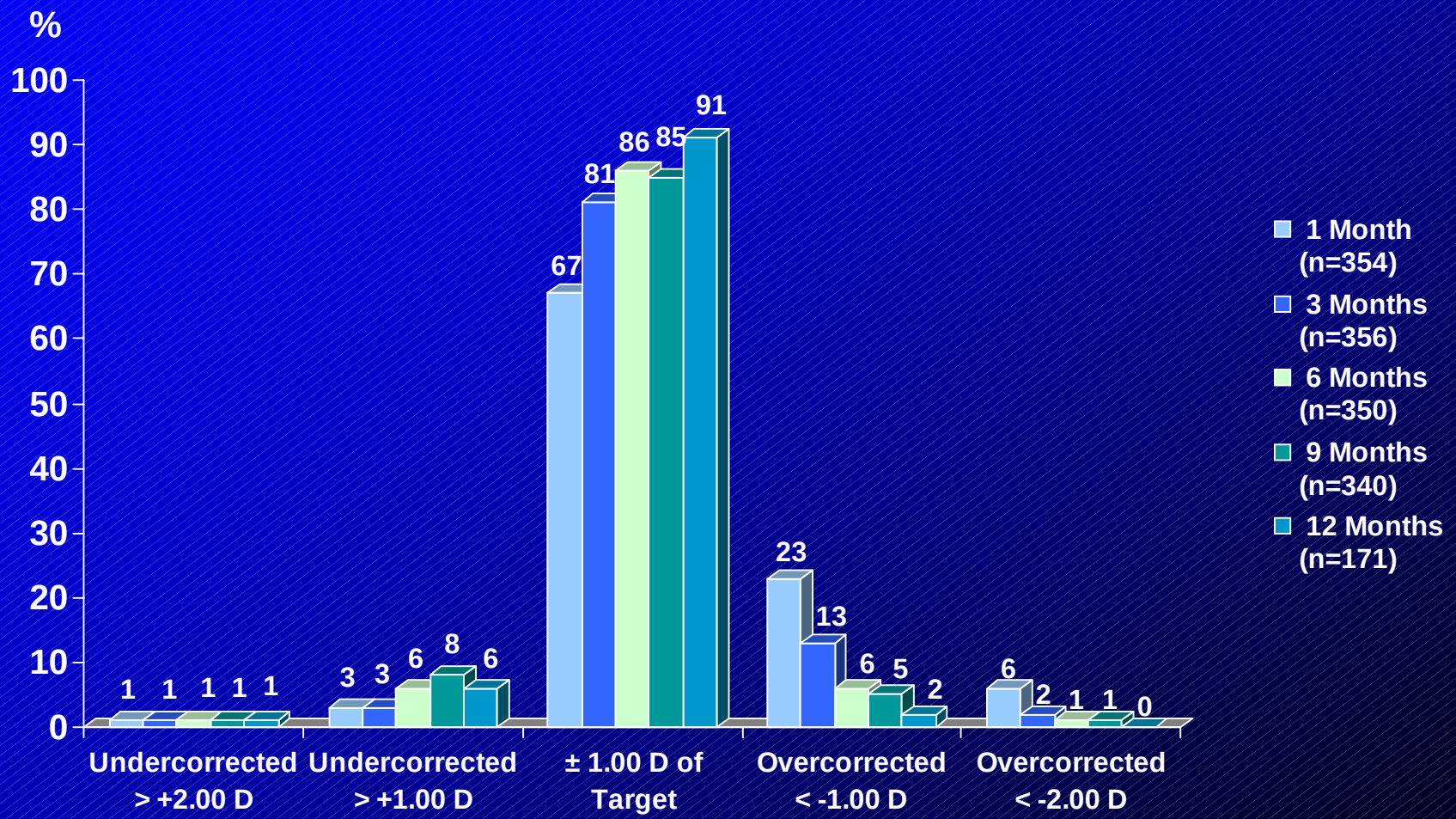
Predictability of MRSE
Eyes Treated with Current Nomogram



Predictability of MRSE
Eyes Treated with Current Nomogram
12 Month Consistent Cohort
(n = 158)

MRSE	6 Months	9 Months	12 Months	FDA Target
± 0.50 D	61%	65%	58%	50%
± 1.00 D	89%	87%	91%	75%
± 2.00 D	98%	98%	99%	-

Predictability of MRSE
Eyes Treated with Current Nomogram



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Effectiveness Parameters
Protocol RCS-001-HYP

- Improvement in UCVA
- Predictability
- **Stability**
- Patient Satisfaction

Stability of MRSE
Patients with All Visits Through 12 Months

Change in MRSE	Between 6 and 9 months (n = 186)	Between 9 and 12 months (n = 186)
Change in MRSE ≤ 0.50 D	88%	85%
Change in MRSE ≤ 0.75 D	95%	97%
Change in MRSE ≤ 1.00 D	98%	97%

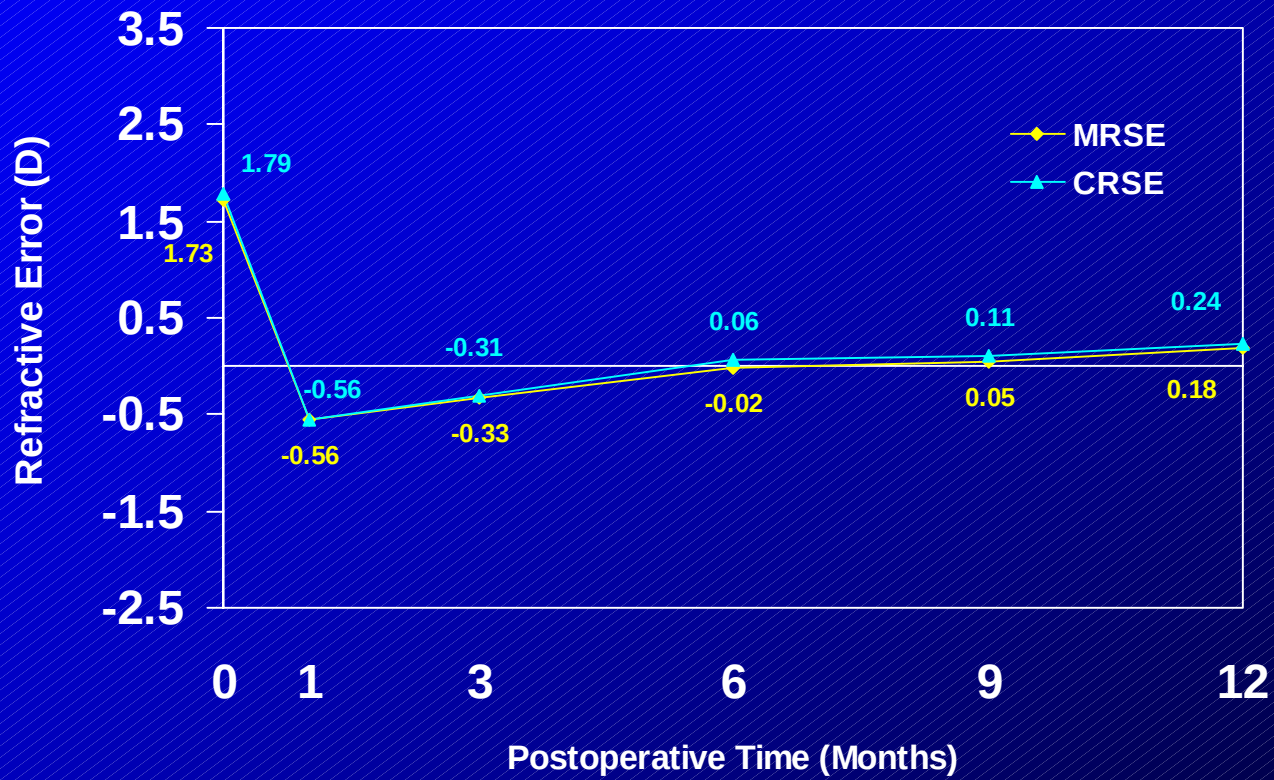
Mean Change in MRSE by Paired Analysis

Per 3 Month Interval	0.08	0.12
By Month	0.03	0.04
95% Confidence Interval	0.02, 0.14	0.06, 0.18
Standard Deviation	0.382	0.386

Stability of CRSE
Patients with All Visits Through 12 Months

Change in CRSE	Between 6 and 9 months (n = 179)	Between 9 and 12 months (n = 179)
Change in CRSE ≤ 0.50 D	81%	88%
Change in CRSE ≤ 0.75 D	96%	100%
Change in CRSE ≤ 1.00 D	97%	100%
Mean Change in CRSE by Paired Analysis		
Per 3 Month Interval	0.09	0.12
By Month	0.03	0.04
95% Confidence Interval	0.03, 0.15	0.08, 0.16
Standard Deviation	0.427	0.320

Mean MRSE and Mean CRSE Over Time
Eyes Treated with Current Nomogram
12 Month Consistent Cohort



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Percent of Intended Correction Remaining
Eyes Treated with Current Nomogram
12 Month Consistent Cohort
(Paired Differences)

	6 Months	9 Months	12 Months
MRSE	106.5%	101.9%	93.0%
CRSE	101.1%	97.8%	89.9%

Effectiveness Parameters
Protocol RCS-001-HYP

- Improvement in UCVA
- Predictability
- Stability
- **Patient Satisfaction**

Patient Satisfaction

	1 Month (n = 356)	3 Months (n = 362)	6 Months (n = 369)	9 Months (n = 357)	12 Months (n = 198)
Very Satisfied	45%	46%	46%	49%	46%
Satisfied	31%	33%	36%	30%	31%
Neutral	16%	15%	9%	12%	11%
Dissatisfied	4%	3%	5%	6%	8%
Very Dissatisfied	3%	2%	3%	3%	4%

Summary of Effectiveness
Eyes Treated with Current Nomogram

	6 Months (n = 350)	9 Months (n = 340)	12 Months (n = 171)	FDA Target
UCVA 20/20 or better	46%	50%	51%	-
UCVA 20/25 or better	65%	74%	73%	-
UCVA 20/40 or better	90%	93%	91%	85%
MRSE ≤ 0.50 D	61%	64%	58%	50%
MRSE ≤ 1.00 D	88%	87%	91%	75%
Stability				
Change in MRSE	Between 6 and 9 Months		Between 9 and 12 Months	
≤ 0.50 D	88%		85%	
≤ 0.75 D	95%		97%	
Mean Change per Month	0.03		0.04	

Safety

Summary of Safety
All Eyes Treated

	6 Months (n = 387)	9 Months (n = 376)	12 Months (n = 203)	FDA Limit
Loss of > 2 lines BSCVA	1%	1%	0%	<5%
Loss of 2 lines BSCVA	4%	3%	<1%	-
BSCVA worse than 20/40	0%	0%	0%	<1%
BSCVA worse than 20/25 if 20/20 or better preoperatively	1%	1%	0%	-
Increase > 2 D cylinder	1%	<1%	<1%	<5%

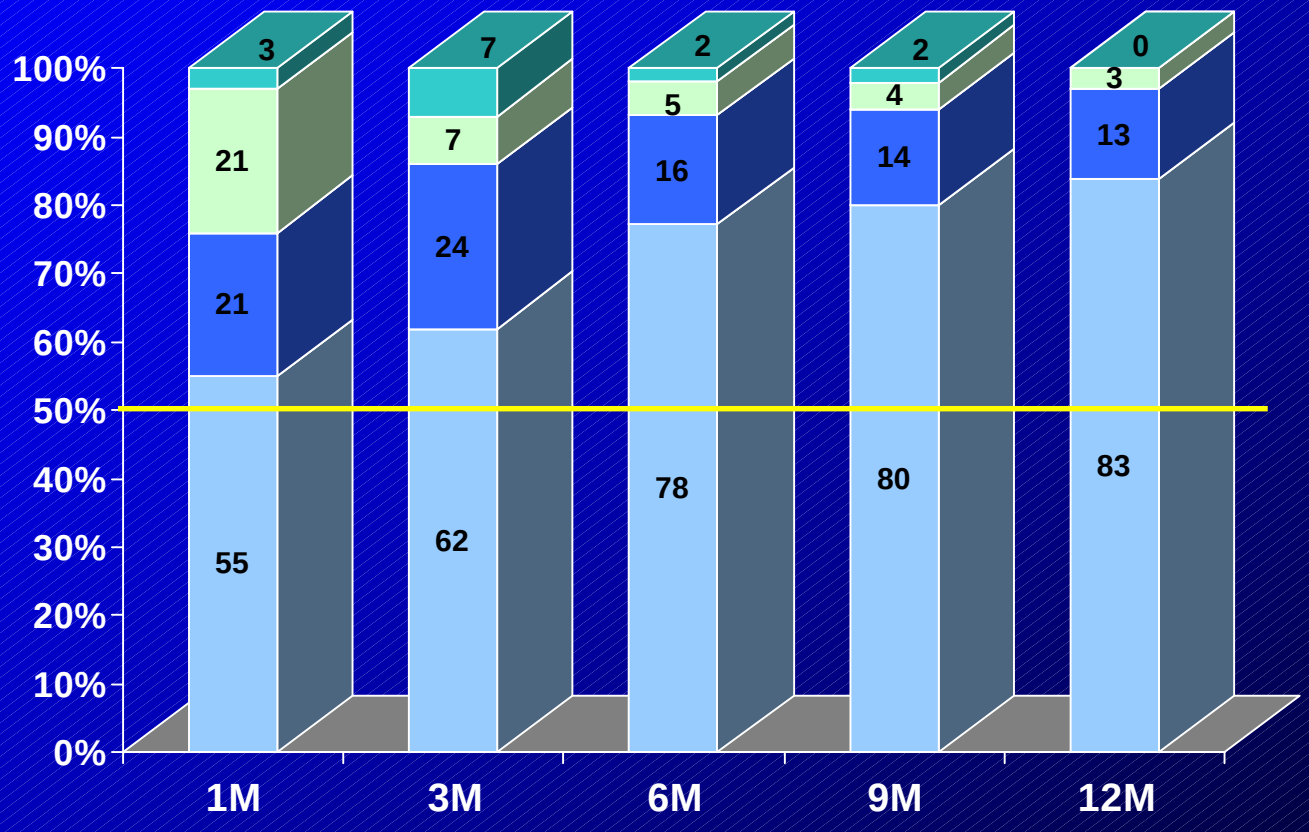
Safety Parameters
Protocol RCS-001-HYP

- **Preservation of BSCVA**
  - **Loss of > 2 lines BSCVA in less than 5% of eyes**
  - **Decrease from 20/20 preoperative to worse than 20/40 postoperative in less than 1% of eyes**
- Induced cylinder
- Endothelial cell loss
- Patient symptoms
- Complications and adverse events

Best Corrected Acuity
All Eyes Treated

	1 Month (n = 390)	3 Months (n = 392)	6 Months (n = 387)	9 Months (n = 376)	12 Months (n = 203)	FDA Limit
Loss of > 2 lines BSCVA	2%	1%	1%	1%	0%	<5%
Loss of 2 lines BSCVA	6%	5%	4%	3%	<1%	-
BSCVA worse than 20/40	0%	0%	0%	0%	0%	<1%
BSCVA worse than 20/25 if 20/20 or better preoperatively	4%	2%	1%	1%	0%	-

Best Corrected Acuity
Cohort of Eyes with ≥ 2 Lines Lost



No eyes worse than 20/40 BSCVA

Safety Parameters
Protocol RCS-001-HYP

- Preservation of BSCVA
- **Induced cylinder**
  - **Induced cylinder > 2.00 D in < 5% of eyes (<1% of eyes per draft ANSI guidance)**
  - **Induced cylinder > 1.00 D reported in labeling for all comparable products for hyperopia treatment**
  - **Induced cylinder ≥ 1.00 D reported at FDA's request**
- Endothelial cell loss
- Patient symptoms
- Complications and adverse events

Absolute Change in Refractive Cylinder
All Eyes Treated

	1 Month (n = 390)	3 Months (n = 392)	6 Months (n = 387)	9 Months (n = 376)	12 Months (n = 203)	FDA Limit
Increase > 2.00 D	3%	2%	<1%	<1%	<1%	<5% (<1%)*
Increase > 1.50 D	9%	5%	4%	2%	1%	-
Increase > 1.00 D	21%	15%	14%	7%	6%	-

* Draft ANSI guidance suggests <1% of eyes should have induced cylinder > 2.00 D

Absolute Change in Refractive Cylinder
9 Month Consistent Cohort
(n = 359)

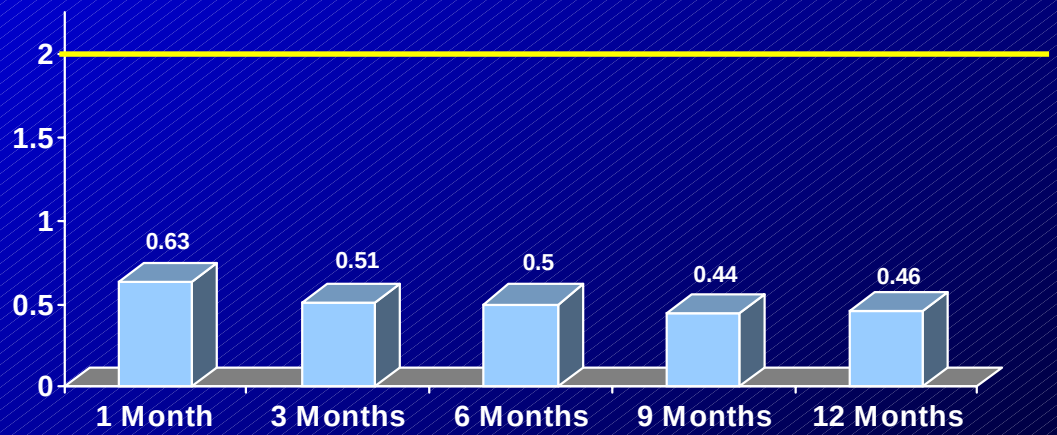
	1 Month	3 Months	6 Months	9 Months	FDA Limit
Increase > 2.00 D	4%	2%	<1%	<1%	<5%
Increase > 1.50 D	10%	5%	4%	2%	-
Increase > 1.00 D	21%	14%	14%	7%	-

Absolute Change in Refractive Cylinder
12 Month Consistent Cohort
(n = 184)

	1 Month	3 Months	6 Months	9 Months	12 Months	FDA Limit
Increase > 2.00 D	4%	2%	0%	<1%	<1%	<5%
Increase > 1.50 D	10%	4%	4%	2%	1%	-
Increase > 1.00 D	21%	12%	13%	8%	6%	-

Mean Induced Cylinder
12 Month Consistent Cohort
(n = 184)

Mean Induced Cylinder	1 Month	3 Months	6 Months	9 Months	12 Months
Mean	0.63	0.51	0.50	0.44	0.46
S.D.	0.68	0.54	0.50	0.45	0.42
95% Confidence Interval	0.73, 0.53	0.59, 0.43	0.58, 0.43	0.51, 0.38	0.52, 0.39



p = 0.0019

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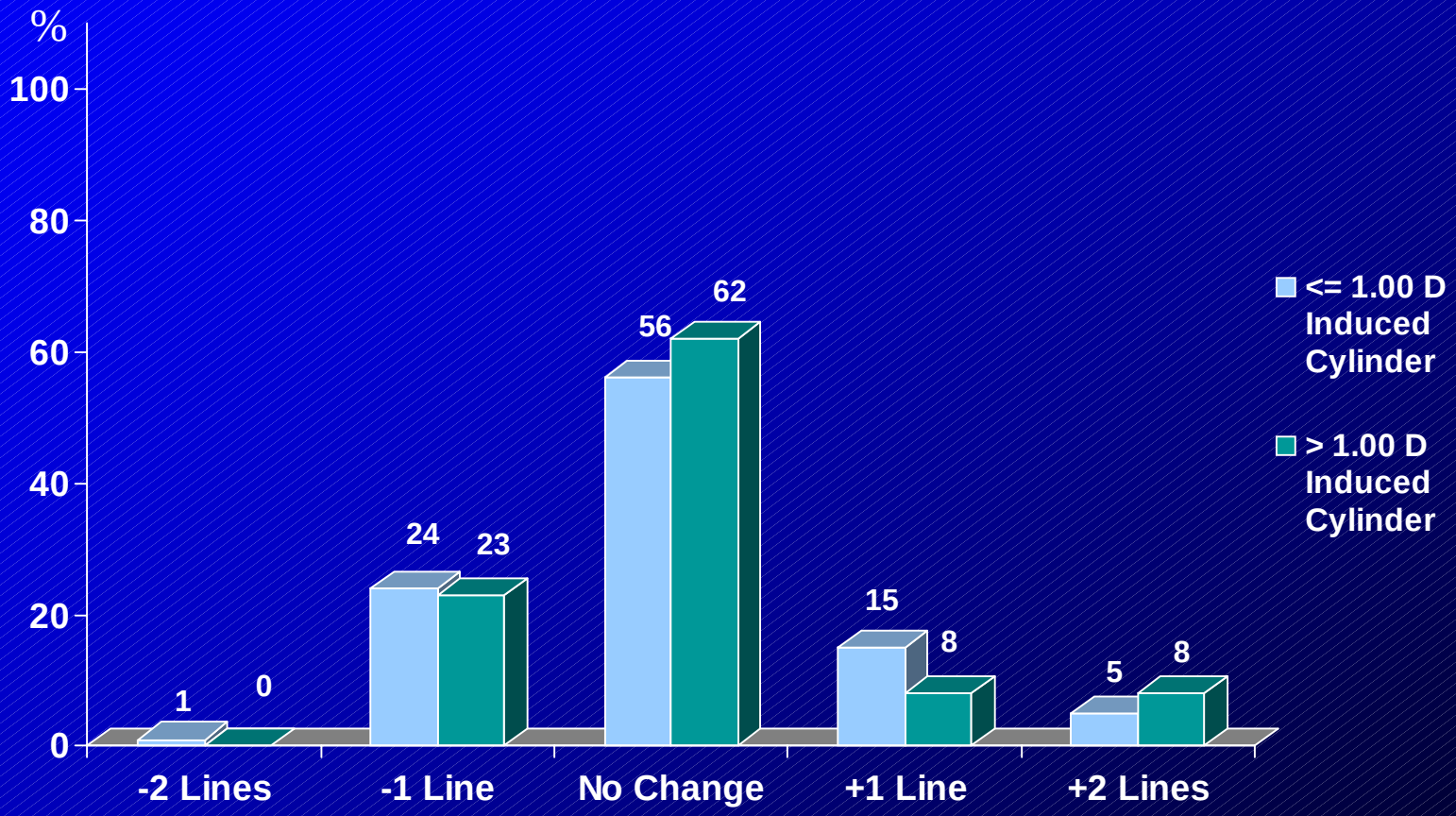
Effect of Induced Cylinder (> 1.00 D) on BSCVA at 12 Months

	Eyes with ≤ 1.00 D Induced Cylinder (n = 190)	Eyes with > 1.00 D Induced Cylinder (n = 13)
Loss of > 2 lines BSCVA	0%	0%
Loss of 2 lines BSCVA	1%	0%
Loss of 1 line BSCVA	24%	23%
No Change in BSCVA	56%	62%
Increase of 1 line BSCVA	15%	8%
Increase of 2 lines BSCVA	5%	8%
Increase of > 2 lines BSCVA	0%	0%

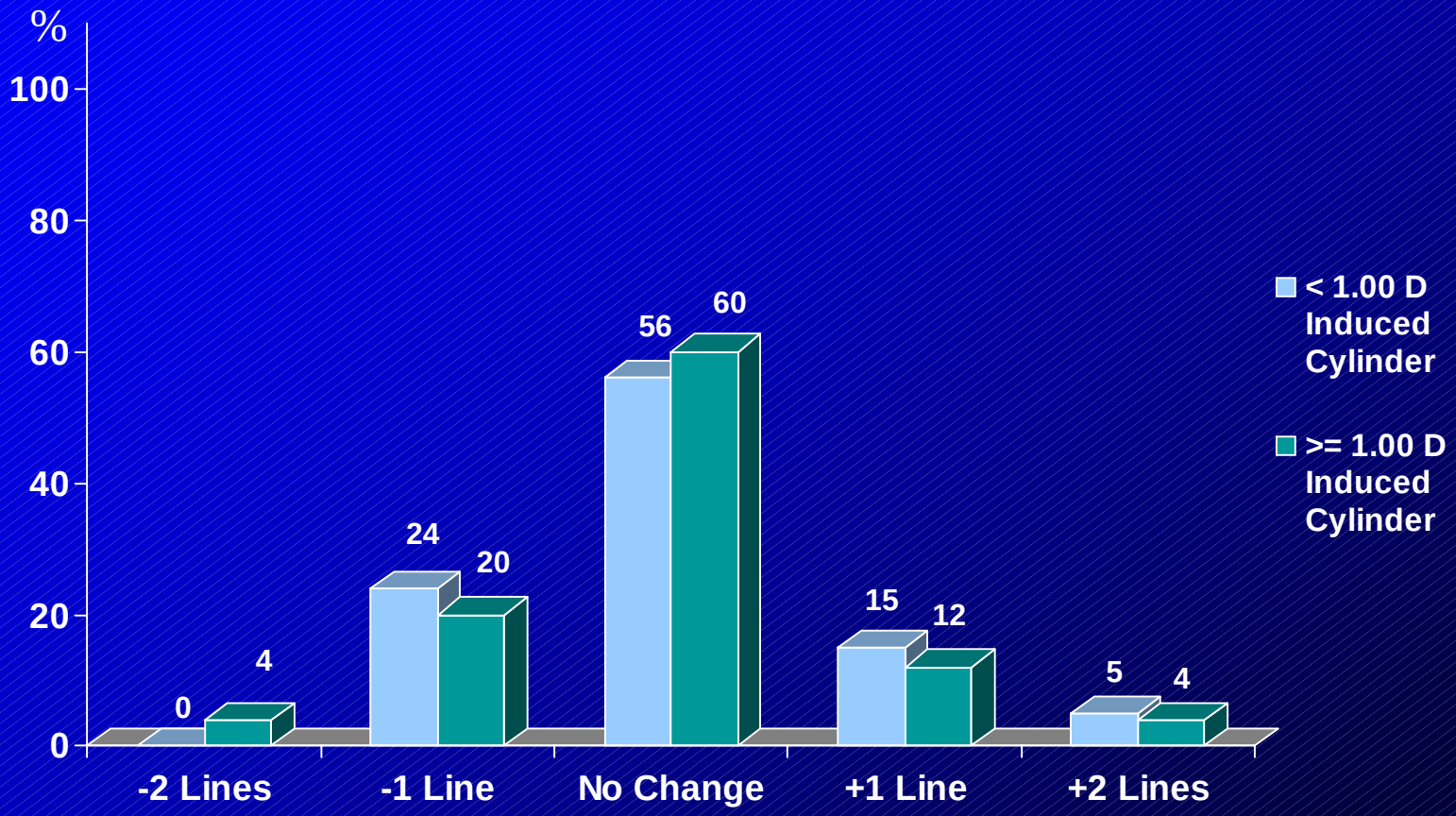
Effect of Induced Cylinder (> 1.00) on BSCVA at 12 Months



Effect of Induced Cylinder (≥ 1.00 D) on BSCVA at 12 Months

	Eyes with < 1.00 D Induced Cylinder (n = 178)	Eyes with ≥ 1.00 D Induced Cylinder (n = 25)
Loss of > 2 lines BSCVA	0%	0%
Loss of 2 lines BSCVA	0%	4%
Loss of 1 line BSCVA	24%	20%
No Change in BSCVA	56%	60%
Increase of 1 line BSCVA	15%	12%
Increase of 2 lines BSCVA	5%	4%
Increase of > 2 lines BSCVA	0%	0%

Effect of Induced Cylinder (≥ 1.00 D) on BSCVA at 12 Months



Effect of Induced Cylinder (> 1.00 D) on UCVA Eyes Treated with Current Nomogram at 12 Months

	Eyes with ≤ 1.00 D Induced Cylinder (n = 162)	Eyes with > 1.00 D Induced Cylinder (n = 9)
Baseline		
Mean UCVA (S.D.)	20/79 (49.8)	20/75 (50.4)
Mean MRSE (S.D.)	1.69 D (0.60)	1.68 D (0.60)
Postoperative		
Mean UCVA (S.D.)	20/27 (14.9)	20/32 (13.7)
Mean Lines of Improvement (S.D.)	4.4 (2.8)	3.3 (2.9)

Effect of Induced Cylinder (≥ 1.00 D) on UCVA Eyes Treated with Current Nomogram at 12 Months

	Eyes with < 1.00 D Induced Cylinder (n = 150)	Eyes with ≥ 1.00 D Induced Cylinder (n = 21)
Baseline		
Mean UCVA (S.D.)	20/79 (49.6)	20/76 (51.6)
Mean MRSE (S.D.)	1.69 D (0.59)	1.70 D (0.66)
Postoperative		
Mean UCVA (S.D.)	20/26 (15.1)	20/31 (12.4)
Mean Lines of Improvement (S.D.)	4.5 (2.8)	3.3 (3.0)

Effect of Induced Vector Cylinder (> 1.00 D) on UCVA Eyes Treated with Current Nomogram at 12 Months

	Eyes with ≤ 1.00 D Induced Vector Cylinder (n = 162)	Eyes with > 1.00 D Induced Vector Cylinder (n = 9)
Baseline		
Mean UCVA (S.D.)	20/81 (51.4)	20/70 (38.5)
Mean MRSE (S.D.)	1.69 D (0.61)	1.70 D (0.56)
Postoperative		
Mean UCVA (S.D.)	20/27 (15.4)	20/30 (11.5)
Mean Lines of Improvement (S.D.)	4.5 (2.8)	3.3 (2.8)

Effect of Induced Vector Cylinder (≥ 1.00 D) on UCVA Eyes Treated with Current Nomogram at 12 Months

	Eyes with < 1.00 D Induced Vector Cylinder (n = 137)	Eyes with ≥ 1.00 D Induced Vector Cylinder (n = 34)
Baseline		
Mean UCVA (S.D.)	20/80 (51.2)	20/76 (44.0)
Mean MRSE (S.D.)	1.68 D (0.60)	1.72 D (0.60)
Postoperative		
Mean UCVA (S.D.)	20/26 (15.8)	20/29 (10.3)
Mean Lines of Improvement (S.D.)	4.5 (2.8)	3.7 (2.8)

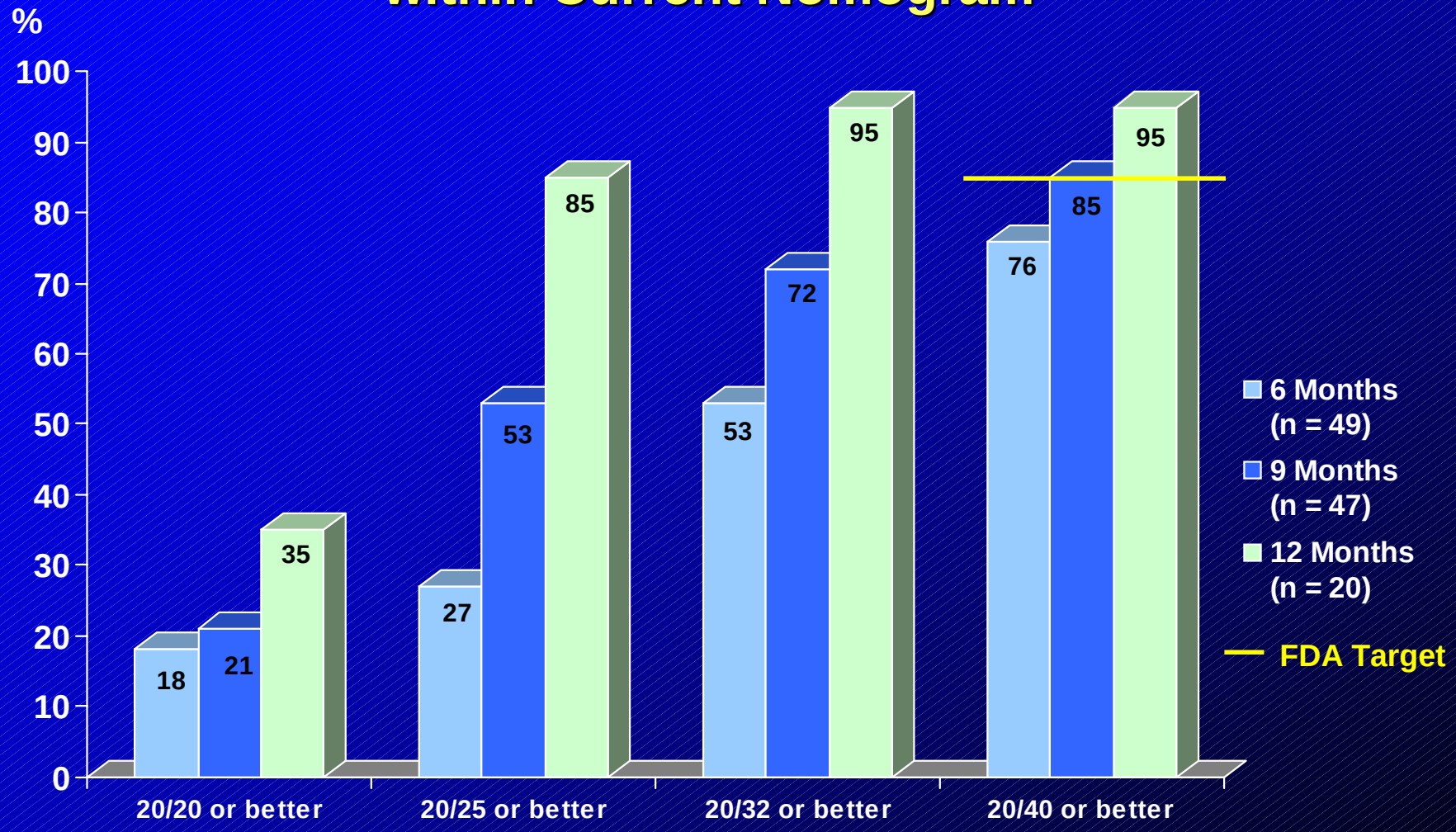
Effect of Induced Cylinder (≥ 0.75 D) and Axis Shift (≥ 30°) on UCVA Eyes Treated with Current Nomogram at 12 Months

	Eyes with < 0.75 D Induced Cylinder and < 30° Axis Shift (n = 151)	Eyes with ≥ 0.75 D Induced Cylinder and ≥ 30° Axis Shift (n = 20)
Baseline		
Mean UCVA (S.D.)	20/79 (49.6)	20/78 (52.3)
Mean MRSE (S.D.)	1.68 D (0.60)	1.75 D (0.64)
Postoperative		
Mean UCVA (S.D.)	20/27 (15.2)	20/30 (12.0)
Mean Lines of Improvement (S.D.)	4.4 (2.8)	3.6 (2.9)

Effect of Induced Cylinder and Axis Shift on UCVA Eyes Treated with Current Nomogram

- Approximately 1 line impact on mean UCVA at 12 months in:
  - Eyes with > 1.00 D and ≥ 1.00 D induced cylinder
  - Eyes with > 1.00 D and ≥ 1.00 D induced vector cylinder
  - Eyes with > 0.75 D induced cylinder and ≥ 30° axis shift
- Correcting for residual sphere using regression models, difference in UCVA not statistically significant (p = 0.82)

Improvement in UCVA Over Time
Eyes with Induced Cylinder > 1.00 D at 6 Months within Current Nomogram



DRAFT

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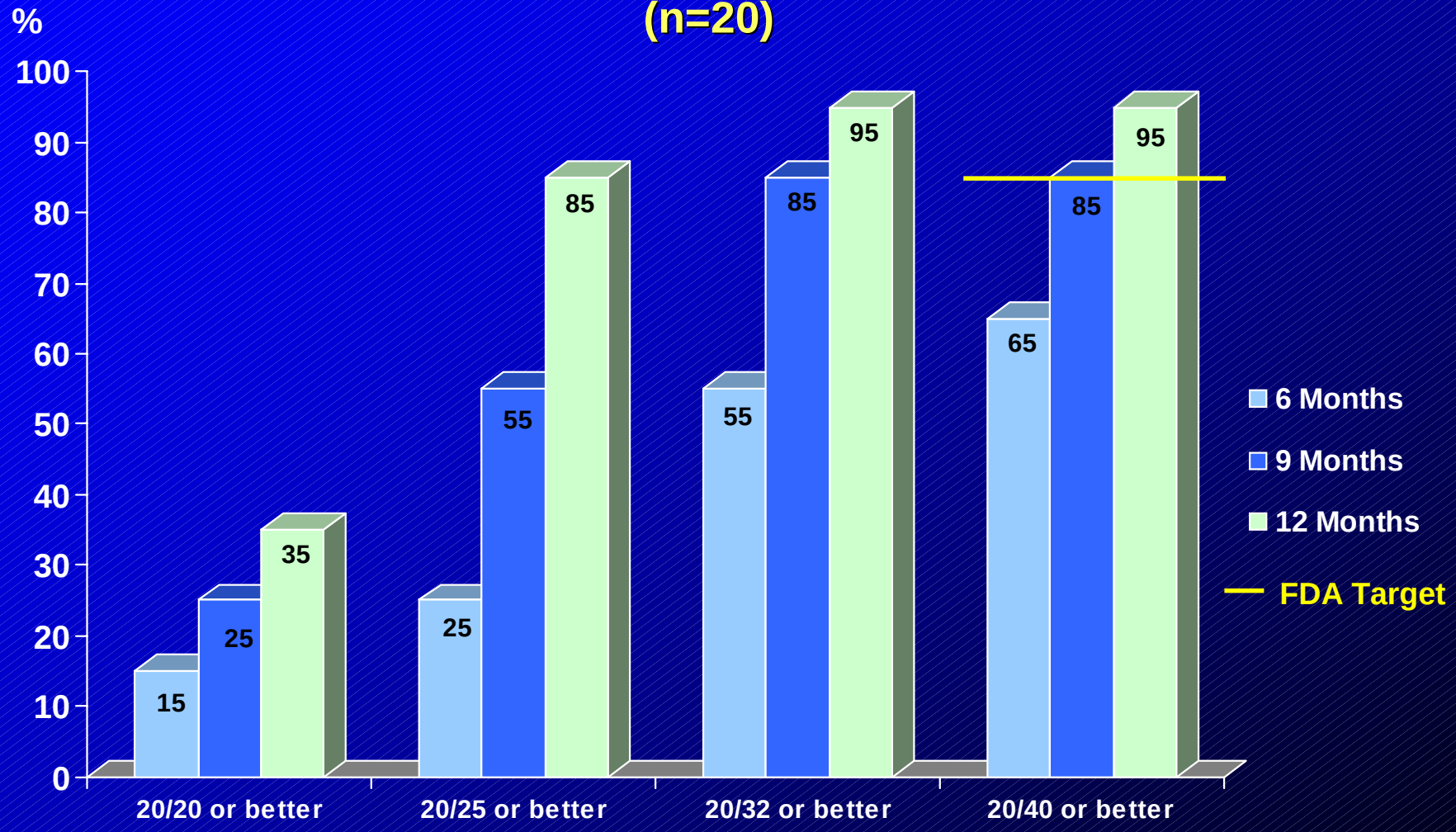
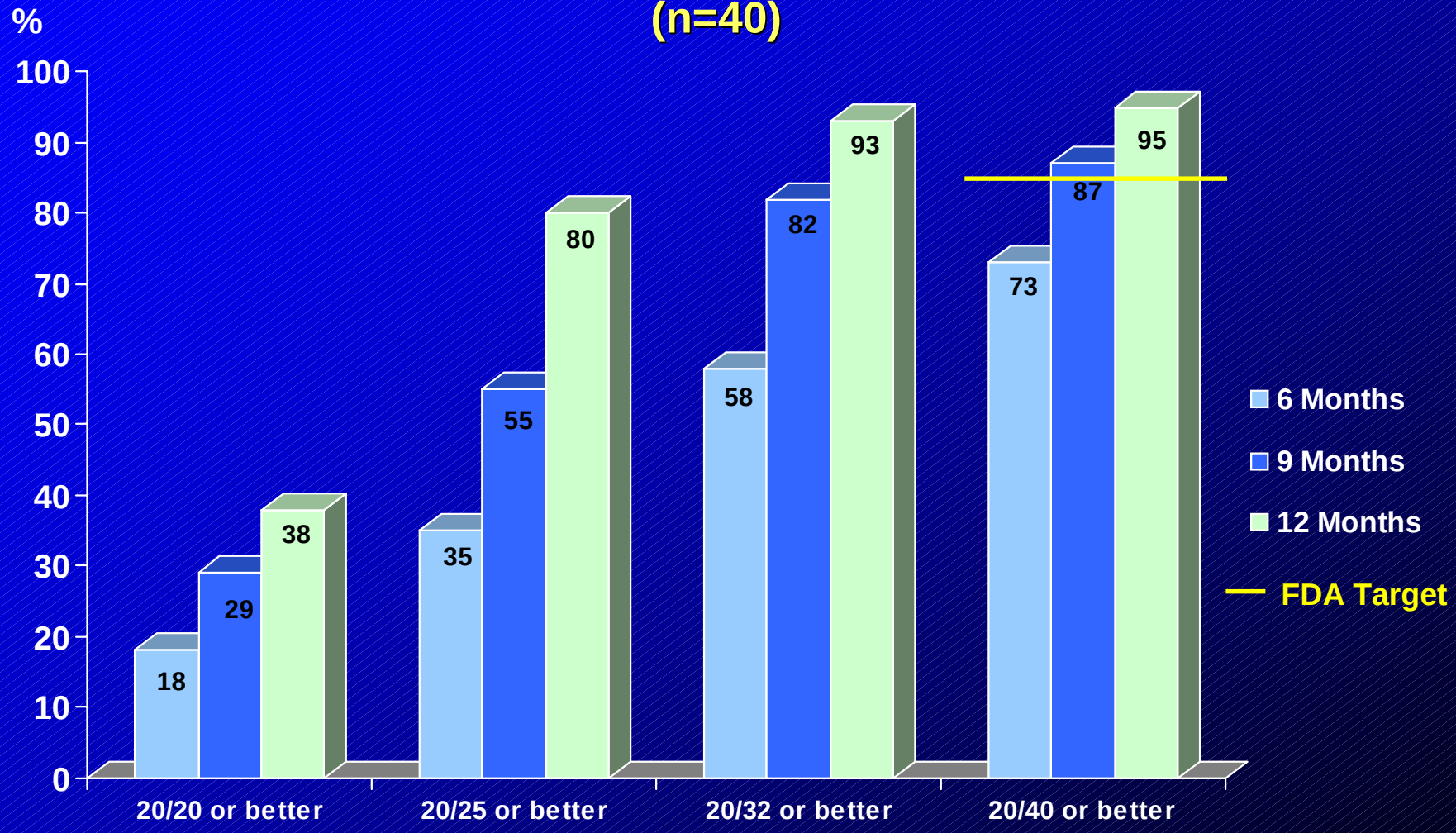
Improvement in UCVA Over Time
Consistent Cohort of Eyes with Induced Cylinder > 1.00 D at 6 Months within Current Nomogram
(n=20)



DRAFT

Refractec

Improvement in UCVA Over Time Consistent Cohort of Eyes with Induced Cylinder ≥ 1.00 D at 6 Months within Current Nomogram (n=40)



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Induced Cylinder Summary

- Meets FDA safety guideline (<5%; <1% proposed)
- Frequency and magnitude diminish over time
- No effect on BSCVA
- When induced cylinder is present:
  - UCVA is affected by approximately 1 line at 6 months and improves over time as induced cylinder resolves
- Level of persistent induced cylinder is low (>1.00 D is 6.4% at 12 months)

Safety Parameters
Protocol RCS-001-HYP

- Preservation of BSCVA
- Induced cylinder
- **Endothelial cell loss**
  - **No more than 10%**
- Patient symptoms
- Complications and adverse events

Mean Endothelial Cell Density
All Eyes in Substudy

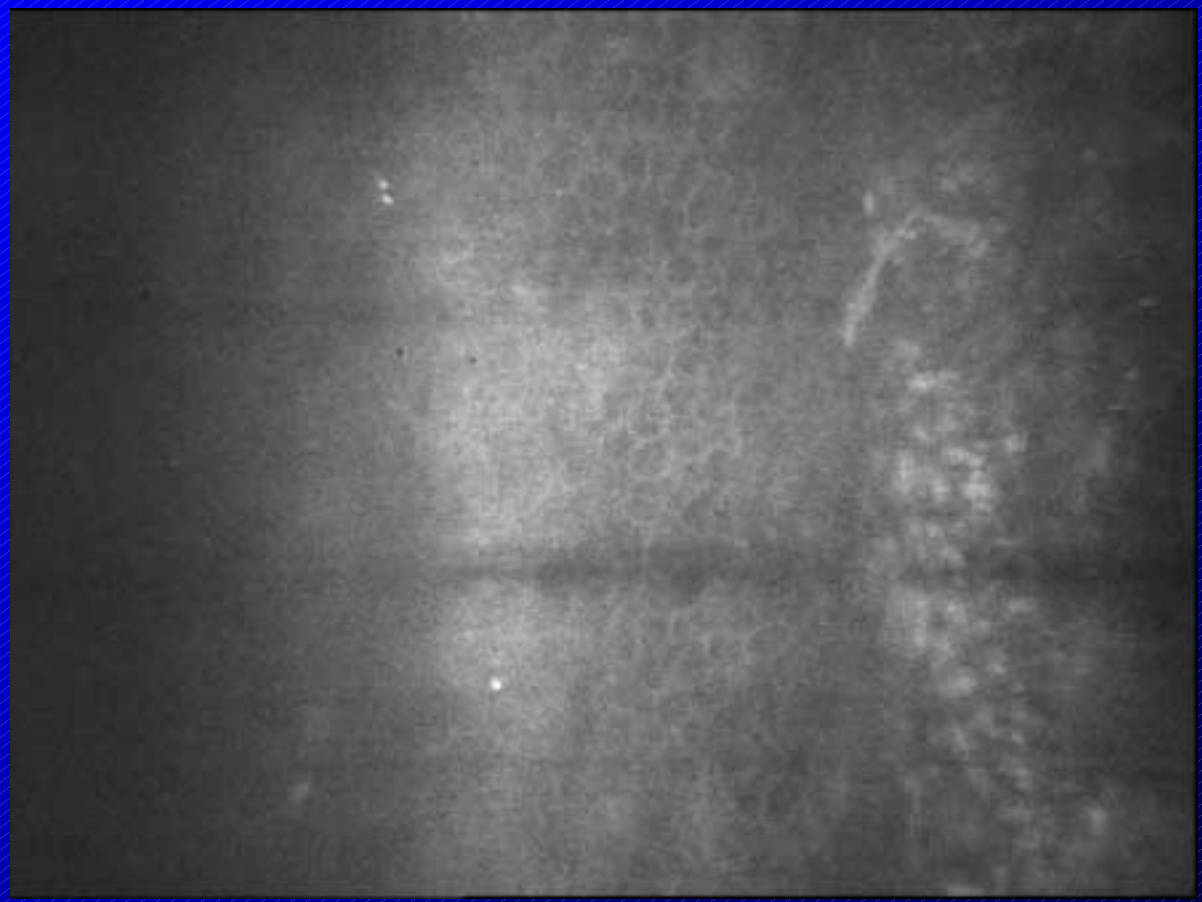
Region		Preop	3 Months	6 Months	12 Months
Central	N	162	127	123	42
	Mean (S.D.)	2686 (160.9)	2730 (163.7)	2727 (153.6)	2683 (163.2)
Mid-Peripheral	N	162	111	108	31
	Mean (S.D.)	2722 (162.0)	2734 (141.3)	2727 (134.4)	2691 (158.4)
Peripheral	N	159	107	104	28
	Mean (S.D.)	2724 (150.9)	2727 (140.2)	2724 (138.4)	2716 (145.3)

Change in Endothelial Cell Density from Baseline All Eyes in Substudy

Mean Change from Baseline (Paired Differences)

Region		3 Months	6 Months	12 Months
Central	N	127	123	42
	Mean (S.D.)	0.31% (4.49)	1.40% (4.19)	1.00% (3.93)
Mid-Peripheral	N	111	108	31
	Mean (S.D.)	-0.61% (3.01)	-0.23% (3.05)	-0.59% (3.62)
Peripheral	N	107	104	28
	Mean (S.D.)	-0.76% (2.96)	-0.41% (3.22)	0.20% (3.52)

Confocal View of Endothelium Below Treatment Spot at 12 Months



Sabry, McDonald & Klyce, 2001

Endothelial Cell Loss
All Eyes in Substudy

- Endothelial cell density
  - No change (within ±1%) in endothelial cell density over the course of follow-up in any region (central, mid-peripheral and peripheral cornea)
  - No polymegathism or polymorphism
  - Radio frequency energy can be safely delivered to the cornea with no effect on the endothelium.

Safety Parameters
Protocol RCS-001-HYP

- Preservation of BSCVA
- Induced cylinder
- Endothelial cell loss
- **Patient symptoms**
  - **Increase of ≥ 5% in moderate to very severe symptoms**
- Complications and adverse events

Patient Symptoms

- Subjective questionnaire was administered at baseline, 1, 3, 6, 9, and 12 months
- Patients were asked to rate the following symptoms as none, mild, moderate, marked, or very severe:
  - Light sensitivity
  - Headaches
  - Pain
  - Redness
  - Dryness
  - Excessive tearing
  - Burning
  - Foreign body sensation
  - Glare
  - Halos
  - Blurred vision
  - Double vision
  - Fluctuation of vision
  - Variations in vision with change in lighting
  - Night driving vision problems

Patient Symptoms

- Symptoms with ≥ 5% increase from baseline in moderate, marked, or very severe at months 6, 9, or 12:

  - Light sensitivity
  - Headaches
  - Pain
  - Redness
  - **Dryness**
  - Excessive tearing
  - Burning
  - Foreign body sensation
  - **Glare**
  - **Halos**
  - Blurred vision
  - **Double vision**
  - **Fluctuation of vision**
  - **Variations in vision with change in lighting**
  - Night driving vision problems

Symptoms with ≥ 5% Increase Over Baseline in Moderate and Marked Categories

Moderate	Preop	6 Months	9 Months	12 Months
Glare	6%	11%	8%	11%
Halos	2%	8%	9%	9%
Fluctuation of Vision	3%	8%	7%	8%
Variation in Vision in Normal Light	4%	9%	8%	6%
Variation in Vision in Dim Light	8%	13%	12%	11%

Marked	Preop	6 Months	9 Months	12 Months
Dryness	1%	6%	5%	2%
Double Vision	1%	6%	5%	3%
Fluctuation of Vision	1%	7%	5%	3%

No significant increase (≥ 5%) in symptoms with very severe rating

Increase from Baseline ≥ 5% in Moderate and Marked Categories

Moderate	6 Months	9 Months	12 Months
Glare	↑ 5%	↑ 2%	↑ 5%
Halos	↑ 6%	↑ 7%	↑ 7%
Fluctuation of Vision	↑ 5%	↑ 4%	↑ 5%
Variation in Vision in Normal Light*	↑ 5%	↑ 4%	↑ 2%
Variation in Vision in Dim Light*	↑ 5%	↑ 4%	↑ 3%

Marked	6 Months	9 Months	12 Months
Dryness*	↑ 5%	↑ 4%	↑ 1%
Double Vision*	↑ 5%	↑ 4%	↑ 2%
Fluctuation of Vision*	↑ 6%	↑ 4%	↑ 2%

* Incidence decreases over time

Safety Parameters
Protocol RCS-001-HYP

- Preservation of BSCVA
- Induced cylinder
- Endothelial cell loss
- Patient symptoms
- **Complications and adverse events**
  - **Adverse events to occur in no more than 5% of eyes**
  - **Any single adverse event to occur in < 1% of eyes**

Complications

- Recurrent corneal erosions in both eyes of 1 patient (<1%)
  - Resolved by 3 months
- Foreign body sensation in 1 eye of 1 patient (<1%)
  - Reported at 9 months, resolved by 12 months
- Pain in both eyes of 1 patient (<1%)
  - Reported at 3 months, resolved by 6 months
- Double/ghost images in 13 eyes of 9 patients (3%)
  - Complaint resolved in majority of eyes (10/13)

Other complications occurring at a rate of <1% include: blepharitis, external hordeolum, viral conjunctivitis, allergic conjunctivitis, bacterial conjunctivitis, meibomianitis, subconjunctival hemorrhage, central striae, central stromal defects, lash loss, echymosis, blurry vision, starbursts, headaches, film over eye, glare, halos, light sensitivity

Adverse Events
Device/Procedure Related

- **Corneal perforation in 1 eye of 1 patient (< 1%)**
  - Resulted from detachment of Teflon stop
  - Healed uneventfully and CK procedure completed successfully 2 weeks later
    - Preop: UCVA 20/40, MRSE +2.00 D
    - 12 month outcome: UCVA 20/16, MRSE 0.00 D
  - Corrective actions implemented

Adverse Events
Device/Procedure Related

- **No RF energy delivered during treatment in 2 eyes of 2 patients (<1%)**
  - Resulted from poor solder joint
  - One eye successfully treated 3 weeks later
    - Preop: UCVA 20/200, MRSE +2.00 D
    - 12 month outcome: UCVA 20/32, MRSE +0.50 D
  - Second eye determined to be ineligible due to previously undetected narrow angles
  - Corrective action validated, implemented and reviewed by FDA

Adverse Events

- IOP > 25 mm Hg in 3 eyes of 2 patients (<1%)
  - One eye of 1 patient had baseline IOP of 25 mm Hg and was therefore ineligible for enrollment
  - Two eyes of 1 patient had increased IOP which resolved without treatment or sequelae
- Mild iritis in 1 eye of 1 patient at 7 days (< 1%)
  - Resolved without sequelae
- Decrease of BSCVA > 2 lines, inferior altitudinal hemianopsia, and optic atrophy secondary to spinal surgery in 1 eye of 1 patient
- Retinal break in 1 eye of 1 patient
  - 18 months post-CK; successfully treated with argon laser
- Non-ophthalmic events include terminal cancer, heart attack, breast cancer, temporal arteritis, hospitalization for tonsillectomy and nasal septum repair

Summary of Safety
All Eyes Treated

	6 Months (n = 387)	9 Months (n = 376)	12 Months (n = 203)	FDA Limit
Loss of > 2 lines BSCVA	1%	1%	0%	<5%
Loss of 2 lines BSCVA	4%	3%	<1%	-
BSCVA worse than 20/40	0%	0%	0%	<1%
BSCVA worse than 20/25 if 20/20 or better preoperatively	1%	1%	0%	-
Increase > 2 D cylinder	1%	<1%	<1%	<5%

Summary and Indications for Use

Refractec

Summary of Effectiveness

- UCVA exceeds FDA target
- Accuracy of achieved vs. intended correction exceeds FDA targets
- From 6 months and beyond:
  - ≥ 85% of eyes demonstrated ≤ 0.50 D change in MRSE
  - Average change per month ≤ 0.04 D
- 93% of intended correction remains at 12 months
- No retreatments performed during study

Summary of Safety

- All performance limits identified in study protocol and FDA guidelines were met
- Preservation of BSCVA established
- Incidence of induced cylinder > 2.00 D meets FDA limit of < 5%
  - Decreases in frequency and magnitude over time
  - No effect on BSCVA
  - Minimal impact on UCVA, which improves over time
- Very low cumulative incidence of adverse events

Indication for Use

- CK treatment for the reduction of spherical hyperopia in the range of:
  - +0.75 to +3.25 D of cycloplegic spherical hyperopia
  - -0.75 D or less of refractive astigmatism
  - +0.75 to +3.00 D cycloplegic spherical equivalent
- In patients with ≤ 0.50 D difference between preoperative manifest and cycloplegic refractions
- In patients 40 years of age or older
- The magnitude of correction diminishes over time with an average loss of approximately 7% of the intended correction at one year